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THE PLAGUE.

A PROSPECT AND A RETROSPECT.

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Studying the history of the Plague in Europe it has been perhaps natural to infer that this dread disease has receded from the civilized areas of the Temperate Zone never to return in epidemic form. We see

* NOTE :—In the following pages I have attempted to bring together matters of direct use to those desiring to have a general idea of our present stand-point in connection with the Plague. I am indebted more especially to :—

The Plague in India, 1896-97, compiled by R. Nathan, Indian Civil Service, IV. Vols., large 8vo. with maps and diagrams. Printed at the Government Central Printing Office, Simla, 1898. Price per set of four Vols., 15 Rs. or £1. The first volume of these more especially gives a most valuable account of the previous history of the Plague in India, description of the Plague, its course and characteristics, and of the measures taken in India to prevent the spread of infection.

Müller & Pösch, Die Pest. Nothnagel's Specielle Pathologie, Vol. No. V., Pt. 4, Vienna, 1900. This is on the whole a most valuable study on the subject, but is in its earlier part based perhaps a little too much upon the work of previous Austrian and German writers, Griesinger for example, and does not sufficiently acknowledge the studies of those of other nationalities—a fact which may in part possibly be explained by the fact that Dr. H. F. Müller, the original author, died of the disease in Vienna before he had revised, or indeed, had nearly completed the work.

Daniel Defoe. A Journal of the Great Plague in London (1665), first printed, London, 1720, reprint, Temple Classics Series, Dent & Co., London, 1900. 75 cents.

Report of the Indian Plague Commission on Haffkine's Anti-Plague Inoculation. Abstr. and editorial in *Brit. Med. Journ.*, Feb. 24th, 1900, p. 455.

Lustig & Galeotti. Remarks on Preventive Inoculation Against Bubonic Plague. *Brit. Med. Journ.*, Feb. 10th, 1900, p. 311.

its last great outburst in England in 1665,* the last outburst in Western Europe at Marseilles in 1721, and in Eastern Europe at Moscow in 1771, and until the closing years of the century in South-Eastern Europe alone—in Turkey—has the plague shown itself epidemically.

But at the present juncture it is right and reasonable to keep in mind that ours may be a false security. We ascribe our immunity to improved hygiene and superior cleanliness, together with (as it would seem from the relative mortality among those of different nationalities stricken of late years in Hong Kong and India) a superior power of resistance in the individual, this resistance or relative insusceptibility being possibly the outcome of better food and consequent more robust health. A more careful study of the facts in relation to the incidence of the Plague may well make us pause. If there is one feature in the history of the disease standing out more than any other, it is the remarkable diversity in the symptoms. In all epidemics there has been the one feature of bubonic enlargements, if not in every case, at least in a considerable proportion of those affected, and the mortality has varied greatly. Now, as in the Black Death, the disease has been of the most virulent septicæmic and hæmorrhagic type; now, as at Bombay in the present epidemic, pneumonic disturbances have been more prominent, and now, as in what the Germans call the "Schlundpest," laryngeal disturbances; indeed, as Cantlie states, a succession of outbreaks in the same city seldom preserves the same type. Bacteriological study of the germ shows us that we are dealing with a microbe peculiarly polymorphic and variable in all its properties. Hence, even if certain races are relatively refractory to the germ in one epidemic, it is well

W. J. Simpson. The Plague in India. *Brit. Med. Journ.*, Sept. 24th, 1898, p. 853.

Haffkine & Bannerman. The Testing of Haffkine's Plague Prophylactic in Plague-stricken Communities in India. *Ibid.*, p. 856.

L. F. Childs. The Pathology of Plague. *Ibid.*, p. 859.

Hankin. Note on the Relation of Insects and Rats to the Spread of Plague. *Ctbl. f. Bakt.* 22, 1897, p. 437.

Hankin & Leumann. A Method of Rapidly Identifying the Microbe of Bubonic Plague. *Ibid.*, p. 438.

Bennett & Bannerman. Inoculation of an Entire Community with Haffkine's Plague Vaccine. *Indian Medical Gazette*, Vol. 34, No. 6, June, 1899.

James Cantlie. The Plague, *The Practitioner*, November, 1899, p. 522. I did not come across this article, having mislaid the reference, until my article was practically complete. In a most clear manner Cantlie takes up the matter very much after the lines here followed and the article is well worth studying by those who wish to obtain a general idea of the nature of the condition written by one, who, in Hong Kong, had abundant opportunity of studying cases.

* As Simpson points out it is not correct to regard this as the last year of the Plague in England—for thirteen years after the great fire in 1666 cases of the disease continued to present themselves.

within the bounds of possibility that, by passage, for example, the germ may have its virulence increased to a point at which racial insusceptibility becomes an absent quality. In the epidemic at Surat from 1684 to 1689, no Englishman was attacked, but in Bombay in 1690, of 800 Europeans only 80 were left, among them 6 civilians, 6 commissioned officers and not quite 40 English soldiers.

What it is that causes variation in virulence and effects we are still very far from knowing—we have, however, to recognize its existence in the Plague as in influenza, and, to give a very present instance, in small-pox. For in this respect nothing can be more instructive than the curiously mild epidemic of small-pox which is now spreading through the Northern States and has made its appearance in Ontario and parts of our own Province of Quebec. Nor again does the fact that two centuries and more have elapsed since the Plague visited Atlantic shores, afford any absolute indication that it has retired never to return. As Dr. Simpson pointed out at the last meeting of the British Medical Association, even in the crowded, painfully insanitary and peculiarly vulnerable eastern cities, while the Plague when once it enters may linger for several years, periods of a century or more may intervene between separate epidemics. Bombay itself was free for 184 years, Moscow, to come nearer home, for 150 years, figures which are not particularly reassuring.

As now the Plague has manifested itself in no uncertain way upon the Atlantic coast of Europe—in Portugal,—not to mention along the Pacific coast, from Japan to the southernmost parts of China; nay more, has assumed an epidemic type in parts of Brazil and the Argentine, we in Northern America must no longer live in a fool's paradise of assured freedom from danger. In saying this I do not wish to pose as an alarmist. As Müller and Pösch point out, in Marseilles in 1721, there were 86,000 deaths out of a population of 247,000, a mortality of 34.8 per cent., and in London in 1665, 68,596 out of a population of 460,000, a mortality of 14.9; Defoe, it is true, gives us the popular impression of his time that this figure is too low and that 100,000 is a true estimate, or a mortality of over 20 per cent. In Canton, on the other hand, in 1894, it is estimated that 140,000 died, or 5 per cent. of the inhabitants. In Bombay in 1896-7, with the more rigorous measures adopted there by the authorities, 19,849 died out of a population of 846,000, a mortality of only 2.3. If in a city so notoriously unsanitary as Canton, and among a people so predisposed to the disease as the Chinese (it is estimated that over 90 per cent. of the Chinese attacked in Hong Kong succumbed), the mortality was only 8 per cent., if again in the continuation of the same epidemic in India, the mortality was brought down by preventive measures to 2.3 per cent.; if again, as the rareness of

hæmorrhagic cases would seem to indicate, the present epidemic is of a relatively mild type, then with our present powers of quarantine and segregation, even did the pestilence gain entry into the country, there is, in my opinion, singularly little chance of its spreading, unless indeed—and this is on the whole unlikely—it suddenly increases greatly in virulence. All that I wish to urge is that reasonable precautions should now be taken to guard against its entrance, and that the present is a particularly favourable time to seek out and remove the weak spots in our hygienic defences, and if, as is the case in Montreal, there are foul and utterly unhealthy areas in the city, now is the acceptable moment for cleansing those areas.

It follows therefore that the quarantine officers at all our ports, both on the Atlantic and on the Pacific, receive the fullest instructions to be on guard against the entrance of infected individuals or infected goods, and that everywhere, but more especially in our seaport towns, the ordinary practitioner be on the alert to recognize the first case, or first symptoms of the disease. We are glad to assure our readers that under the able direction of Dr. Montizambert, all official precautions are being taken. Only within the last few days a bacteriological laboratory has been inaugurated in connection with the quarantine service at Victoria, B.C., and Dr. Charles Higgins, Assistant Pathologist and Bacteriologist to the Department of Agriculture, a thoroughly capable and reliable official, has been placed in charge. At the Atlantic ports also care is being taken to obtain sure diagnosis and segregation of any suspected cases. It is opportune, however, to collect here into a brief and succinct form the main characteristics of the disease and the means of diagnosing and of preventing the spread of the same, so that the general practitioner be not perchance caught napping.

THE NATURE OF THE PLAGUE AND ITS CHARACTERISTIC SYMPTOMS.

What then is the plague? It is a disease caused by infection by a specific bacillus, manifesting itself more particularly as a malignant lymphadenitis, and its characteristic symptom, that which distinguishes it from all other epidemic diseases, is the production of buboes. Just as in cholera, the mucous membrane of the intestine is the tissue of election, and in small-pox the skin—so in the Plague it is the lymph glands which are especially picked out, and here, I may add, it is that the specific bacteria of the disease are to be detected in profuse abundance. But again, just as one may occasionally come across a case of typhoid in which there are no enlarged Peyer's patches, so occasionally, a case of plague presents no enlarged subcutaneous lymph glands—while, apparently more frequently than is the case with typhoid, the

disease may take on the pneumonic type.* For our present purposes, these cases, which are peculiarly fatal, may, I think, be neglected. The general history when the pestilence first reaches a country, is that the earlier cases tend to be mild and indefinite and of the bubonic type. This is well brought out in Defoe's classical account of the Great Plague in 1665, of which I here note a new and excellently printed edition in the now familiar "Temple Classic" Series. Like other epidemics this tends to begin insidiously, and as often the earliest cases of cholera appear to be nothing more than a somewhat more severe diarrhoea than normal, so the Plague may show itself first as a development of buboes, clearly non-venereal in origin, accompanied by little or but transient disturbance. As pointed out, I believe, by Cantlie, cases of slight fever accompanied by glandular enlargement were noted at Hong Kong before the plague was recognized there—and Simpson gives full details of similar cases in the Shropshire regiment which came to Calcutta from Hong Kong. The condition spread to other soldiers who had never been in Hong Kong and eventually terminated in cases of typical Plague.

It is not surprising that the heads of the Indian Medical Service refused to acknowledge that they were here dealing with the genuine disease. What I wish to point out here, is that cases of non-venereal bubo occurring in the out-patient room or in private practice, deserve now-a-days to be investigated and followed with particular care—more especially if those cases be accompanied by slight fever and a white coated tongue, red at the tip and edges. In short, any case of fever accompanied by marked glandular enlargements in either groin, axilla or neck, deserves thorough investigation.

The general experience of the Bombay epidemic is that buboes which

* Cantlie distinguishes the following varieties of type :

1. The *Bubonic* form, "as a rule the first outbreak of Plague in a community is bubonic in type whatever it may become afterwards."

2. *Pneumonic*.

3. *Intestinal*, in which an intestinal flux occurs consisting of diarrhoea at the onset to be followed later by the appearance of blood, mucus and epithelium in the stools.

4. The *Cerebral*, in which delirium, often apparently of a suicidal type sets in early, with twitchings, tonic and clonic spasms, especially in children, loss of consciousness and deafness are more than occasionally manifest.

5. *Puerperal*, in which uterine hæmorrhage and miscarriage are the prominent features.

6. *Pestis Siderans*, rapidly fatal cases in which the usual clinical signs have not time to develop.

7. *Typhus Type*, resembling malignant typhus ; in the Tropics not unfrequently the symptoms of the two diseases are almost identical, even to the skin eruption.

8. *Pestis Ambulans*. A mild type of the disease frequently included under the heading of,

9. *Pestis Minor*, sporadic or even epidemic outbreaks of adenitis going on to suppuration with, however, little constitutional disturbance.

have gone on to well-developed suppuration, yield pus free from plague bacilli and as the only sure means of diagnosis in a doubtful case is the bacteriological, the study of a suppurating bubo is likely to yield no certain results. Examination must be made before suppuration develops and if this is not possible, recourse should be had to the agglutination test, for in the later stages of the disease the blood gains agglutinating properties. A drop of blood collected, as in Wyatt Johnston's method for typhoid fever, and sent to a bacteriological laboratory, may thus afford valuable information. In the earlier stage of the bubo, as already indicated, and in the surrounding sero-sanguinolent fluid abundant bacilli are present.

Passing from these cases of "Pestis minor," before indicating the main symptoms of the more virulent disease, a few words may be said with regard to the specific microbe and to the essential nature of the plague process.

THE PLAGUE BACILLUS.

The bacillus which was discovered by Kitasato during the epidemic in Hong Kong in 1894, has been abundantly proved to be the specific cause of the disease. It is present in large numbers in the buboes in the early stage of the disease and in the hæmorrhagic cedematous fluid surrounding them. It is from these that the bacilli can be obtained in the greatest abundance and diagnosis be made without difficulty. In well marked cases it is present also in the blood but here the individual bacteria are few and far between in any given specimen, and thus the failure to discover them in the blood is not by any means a positive indication that the individual is not suffering from the disease.

These bacilli are short and thick, with rounded ends and when grown outside the body frequently occur in short chains and from the deeper staining of the ends tend to appear like diplococci; they do not stain by Gram's method. They grow best at blood temperature upon all the ordinary media. The most characteristic growth is in slightly alkaline peptone broth, and more especially, as Hankin has pointed out, when a little butter fat has been added. The bacilli tend to grow round the fat droplets upon the surface and falling down form long festoons or stalactites, the old growths gradually accumulating at the bottom as a granular or grumous deposit, while the medium remains clear. Grown outside the body involution or degeneration forms show themselves with fair rapidity, and as Hankin points out, this tendency to involution may be made a means of rapidly identifying the microbe. If this is inoculated upon agar containing from 2.5 to 3.5 per cent. of common salt, involution forms will be found in an unmistakable way after a lapse of 24 hours. Hankin and Leumann have cultivated a large num-

ber of other microbes under like conditions and in none of them have they had any approach to the appearances presented by the Plague bacilli under these conditions of growth in salted media.

The bacillus is pathogenic for rats, mice, guinea pig, rabbits, flies and other insects, and is rapidly communicated from one animal to another. After death the bacilli are found in all the organs. Furthermore, it is rapidly communicated from one animal to another. Though I am inclined to think that too much is being made of this conveyance of the disease by means of rats, nevertheless, the relationship of disease among these animals to plague in man has been noted for centuries, nay more, as I previously pointed out in this Journal,* the fact of this relationship carries us back to about 1141 B.C. in our knowledge of the existence of the Plague.

A curious fact has recently been pointed out, namely, that the known danger of handling rats that have died of the disease extends at most for 24 hours; after this period they may be handled with impunity, and it is indicated, with a fair amount of probability, that the infection is by means of the fleas and parasites on the rat's body which pass on to the hands and clothes of those taking them up immediately after death, which also in a few hours have deserted the bodies, these becoming, therefore, relatively harmless.

THE DISEASE PROCESS.

We have, it would seem, to deal with an infection occurring most frequently through the skin. It is remarkable that the primary seat of infection is in the majority of cases, unrecognizable. Light is thrown upon this peculiarity of the disease by certain observations of Albrecht and Ghon, that the disease may be induced in susceptible animals by merely rubbing some of the virus over the skin, and this even when it has not been previously shaved. In such experiments no marked local reaction need result, but the animal rapidly succumbs. As Hankin (private communication in 1897), Childe and others have pointed out, in some cases a minute reddened papule going

* Adami—Montreal Medical Journal, Vol. 24, 1896, p. 995. Since writing that account of the Plague among the Philistines, and the Trespass Offering of the Golden Emerods (buboes) and Golden Mice, I have learnt that the Hebrew word translated mice, is one which equally refers to rats and small rodents in general. While it is true that mice like rats are affected during Plague epidemics, their wandering out to open places and dying there is not so marked as it is with rats, and thus, if this word refers to rodents in general, the case in favor of the disease among the Philistines and Israelites being the Plague, becomes even stronger. Probably as a result of my note on the matter being contributed in a "Retrospect" it has been largely overlooked. I was not a little interested to come across in last Saturday's *Evening Post* (New York), April 14th, an announcement heralding this same antiquarian discovery by the same writer of a paper presented recently to the Royal Society of New South Wales!

on to vesiculation, may be seen in the very earliest stages in the cutaneous area associated with the first lymph gland which shows enlargement (primary bubo) and here may be found abundant bacilli. One of Childe's cases is peculiarly instructive: The small unopened papule with sero-pus in its apex was found exactly upon the mid-dorsal aspect of the glans penis; from it pure cultures of the bacillus were obtained, which injected into a rat, caused its death from plague. In this case the inguinal glands *on both sides* were equally affected and enlarged to the size of walnuts. Hankin has communicated to me a somewhat similar case. Rarely the local reaction at the point of infection is more pronounced and a primary carbuncle with hæmorrhages, necrotic centre and surrounding œdema, has been observed. It would seem that Roux's statement is well based, that the more marked the local reaction, the less virulent the disease and the more favourable the prognosis; the virulent germ is not arrested locally, but is conveyed rapidly to the nearest lymph gland and there sets up the inflammatory reaction which results in the development of the primary bubo.

I am, I take it, wrong in saying the nearest lymph gland, for as in the case of Professor Aoyama, the primary vesicle may be upon the hand, the primary bubo in the axilla (with in his case a somewhat rare intervening lymphangitis). It is indeed not a little remarkable how rare are buboes in the popliteal and cubital spaces. Either the main body of lymph from the extremities does not traverse the glands situated in these spaces, or the different lymph glands exhibit varying reactions to the virus. Certain it is that the glands of the groin and of the axilla are far and away the commonest seats of the primary bubo.

Next most common are the cervical glands, an indication that infection may be through the tonsils, the mouth, or the nasal mucosa. Feeding animals with the pest bacilli leads much more frequently to the development of cervical buboes than to enlargement of the mesenteric glands. I shall refer later to infection through the lungs.

In general, the course of the disease may be described as, (1). Local infection unrecognizable, or if recognizable accompanied by a minimal local reaction. (2). Affection of one or more of the group of lymph glands associated with the area of local infection, which affection at first sets up at most local swelling and pain, but no general reaction, *i.e.*, the moment general symptoms set in the bubo is already a prominent feature. (3). Following rapidly upon this local production of a bubo there is generalization of the disease—diffusion of the bacilli and their products into the blood and supervention of general symptoms.

SYMPTOMATOLOGY.

I may now rapidly note down, the main symptoms of the disease:—

I. In general, the disease shows itself with remarkable suddenness; there is an initial severe rigor, intense headache with giddiness suddenly supervening upon apparently perfect health, and rapidly developing prostration. More rarely there is a prodromal period in which the patient feels somewhat out of sorts with slight headache, nausea, feeling of weakness in the limbs and it may be some pain, more especially upon pressure in the region where the primary bubo will eventually become manifest. The intense headache and rigors are accompanied by a dry hot skin, the eyes become sunken, the features drawn, and soon a typhoidal state develops with or without coma.

II. There is definite but not particularly high fever rising rapidly to, generally, from 102 to 104°F., with tendency to remissions in the early morning hours and exacerbations in the late afternoon and evening hours, the temperature, however, may never exceed 101°. In favourable cases there may be resolution by lysis, the curve resembling somewhat that of typhoid convalescence, or more rarely by crisis. Septic complications may induce a characteristic curve.

III. Save in the fulminant and pneumonic cases, in which a primary bubo tends to be absent, a bubo, most often in the groin, next most frequently in the axilla, or again less frequently in the neck region,—is to be made out from the very beginning of the illness. An inguinal bubo is most common in adults, a cervical in children. This is, indeed, the “token” of the disease. It is painful on pressure, surrounded by an oedematous area, may be only just palpable, but in general is from the size of a walnut to that of a goose’s egg; the skin over it is glazed and may be hæmorrhagic and vesicular. In the immediate neighbourhood of this primary bubo there may be other markedly enlarged lymph glands (primary buboes of the second class as they are termed by Albrecht and Ghon), enlarged as a consequence of direct infection through the lymph and showing similar characters. Only very rarely are there bilateral primary buboes (*e.g.* where infection has been through the integument in the midline of the body). Eventually there may be a general enlargement of all superficial lymph glands, *secondary* buboes; but these again, with very rare exceptions, do not show the same large size and surrounding infiltration and hæmorrhages seen in the primary. They are evidently due to infection of the glands from the blood stream after the germs have become generalized.

IV. Other “tokens” are carbuncles and cutaneous hæmorrhages. The latter are only seen in very malignant cases, as in the “Black Death,” the former may be primary, at the seat of what is evidently the primary infection, or secondary, due like the secondary buboes to general blood infection.

V. Nervous disturbances are marked, but are very variable. The

preliminary headache and giddiness have already been mentioned. The rest, in the main, are those of the "typhoid state." The giddiness is accompanied by a characteristic walk, as of a drunken man, that of cerebellar ataxia. Sensory disturbances show themselves in the main by apathy, sleepiness or, it may be, complete coma. The speech is slow, and "far away," the eyes dull and heavy; delirium of a prolonged type, colourless (as Müller expresses it), as of a man enacting a prolonged dream, talking and gesticulating to imaginary individuals, is met with. And very characteristically this delirium often leads the patient to get out of bed and wander about aimlessly in the house or street. Defoe gives vivid pictures of this form. While the delirium may be acute, and sometimes of the suicidal, it is most often of the quiet form.

VI. The pulse from being, according to Aoyama, large and full and dicrotic at the start, soon becomes rapid, 120 and more; in cases of unfavourable prognosis, small and of low tension; in fatal cases Müller frequently counted it at 200 and over, indeed, as a case progresses to a fatal termination, the rate becomes more and more rapid. As Müller points out the plague virus is a strong cardiac poison and the pulse indicates very largely the potent effect of the disease in inducing cardiac weakness. Death would in the main seem due to direct action of the poison upon the heart muscles, or it may be, though this is not so likely, upon the cardiac nerves.

VII. Beyond epistaxis and pharyngeal (tonsillar) ulceration, the upper air passages are usually found unaffected. The lungs are usually intact, though there may at times be a certain amount of bronchial catarrh from the third or fourth day. The Bombay epidemic has, however, clearly proved the existence of one special type of Plague—pneumonic Plague. This form was first clearly differentiated by Forbes in the Pali plague of 1838, if not by Gilder at Ahmedabad in 1820. And there can be no doubt that the Black Death, the most terrible visitation known in history, was this most malignant form of the disease. At Bombay, L. F. Childe first called attention to its existence. Just as we have two main forms of anthrax in man, malignant carbuncle in which the primary infection is through the skin, and wool sorters disease (pneumonic anthrax), so it is with this disease. The patients present no very prominent pulmonary symptom; there is a cough but not very frequent, the expectoration, however, is blood stained and contains abundant bacilli—and soon there is extreme dyspnoea with cyanosis. So far, in the relatively few cases that have been studied, there have been pleuritic pains but no accompanying herpes. In ordinary Plague the respirations may rise to 30 or 40—in this condition they may be as frequent as 60 to 75. The condition is one of a lobular pneumonia and the auscultatory and other signs correspond.

What is noticeable is that the lips are dry, while, according to several observers, the tongue has a whitish or chalky surface with reddened tip and edges and it tends to be swollen. The tonsils in general are markedly swollen and reddened—more rarely they are ulcerated. It must be remembered that the frequency of cervical buboes in children would seem to be related to more frequent infection through the mouth or tonsils, even more than through the nose. The gastric juice appears to prevent primary infection of the intestines. Persistent vomiting is by many regarded as an unfavourable sign.

VIII. Wilm, at Hong Kong, is the only authority who has recorded primary plague affecting the abdominal digestive tract; other authorities are inclined to regard this as peculiarly rare, if not non-existent. With regard to the stools they are either regular or more often there is a tendency to constipation. Cantlie, Wilm and others found diarrhoea frequent at Hong Kong in the earlier stages with blood and mucus present. At Bombay this was rare.

IX. The liver, spleen and kidneys present no constant disturbances recognizable clinically. According to Yamagiwa and other recent observers, the amount of urine is diminished, albumin is generally present, but in relatively small quantities. The urine is often of a dark colour and contains indican (Aoyama), chlorides are diminished. There would in short appear to be a not very marked febrile nephritis. Bacilli have frequently been found in the urine—hæmaturia is rare.

PROGNOSIS :

Cases are on record in which the individual without previous warning has dropped down as if struck by lightning (? heart failure) several in which death has resulted within four or five hours from the first onset of symptoms. Death most frequently occurs within five days. If the patient survives for six days, the prognosis becomes on the whole favourable, being distinctly favourable after the eighth day is passed. Where death occurs late, or in the second or third week, it would seem that secondary septic infection is mainly responsible. Suppuration of the buboes, which many hold to be a favourable sign, does not by any means indicate secondary infection—for the Plague bacillus itself can induce true pus production.

TREATMENT :

No specific treatment by drugs has as yet been discovered. Digitalis and cardiac tonics have not been found to effect any definite improvement; nor again the surgical removal of the primary bubo. Already when this becomes noticeable the bacilli are abundant in the surrounding cedematous and hæmorrhagic infiltration. The seat of infection is so often

unrecognizable and when present is so indefinite that little in the way of cure is to be expected from excision.

In this last epidemic as in those of centuries ago, the physician has found himself wholly at a loss to influence the disease by means of drugs of any order; at most an attempt can be made to mitigate individual symptoms. One exception must, however, be made to this sweeping statement; the researches and observations of Yersin have undoubtedly shown that in a certain number of early cases—in which the treatment has been begun at an early stage—the injection of plague serum is effectual. This serum is obtained by accustoming a horse to stand larger and larger dose of the toxins of the Plague bacillus and eventually of the most virulent bacilli themselves. But no small difficulties stand in the way of successful treatment by this method. In the first place, the process of successive injections of horses takes a very long period; in the second place, it would seem clearly that individual horses vary greatly in the amount of antitoxic substances which they develop in their serum and to these two causes we must largely trace the ill success that followed the use of the serum sent from the Pasteur Institute, Paris, to Bombay. In the third place, the amount of serum obtainable from an individual horse is limited and as a consequence the serum is costly and difficult to obtain in any large quantity. In the fourth place, as already hinted here, as is true also in connection with the diphtheria serum or antitoxine, success or ill-success depends very largely upon how soon after the supervention of symptoms the treatment can be applied. In Plague, the infection becomes so rapidly generalized throughout the system, that in severe cases, however soon the treatment may be commenced the infection of the body in general is already so intense and the amount of toxins produced so extreme that, whether the antitoxines directly neutralize the toxins or whether they serve as stimulants, stimulating the tissues to react against these toxins, no amount of serum is adequate to arrest the progress of the disease. However, it must be remembered that we are only at the beginning of serum therapy and it may still be that within the next few years great advances will be achieved. So far, it is true, it is only along these lines that at the present moment we recognize any possible means of influencing the course of the disease.

PREVENTIVE MEASURES :

It is not necessary here to lay down the duties of the quarantine service and to point out the means whereby the disease can be hindered from entering the country. But a few words may be said concerning those points in which the Plague possesses characters of its own demanding for it special treatment. In the first place, it is a peculiarly contagious disease; its spread is rarely by the water or again by the

air, whereby I mean to indicate that the bacilli exposed to the air and sunlight are very rapidly destroyed, and as a matter of fact it is only those in the very immediate neighbourhood of patients, those brought into contact with them or with diseased animals (rats, mice, cats), or again with the soiled linen of patients—who are likely to contract the disease. Thus is it that at the beginning of an epidemic the spread is characteristically from one member of a household to another and from one household to another according to the intercourse between the households. It was found in India that if an infected house be left untenanted for twenty days with windows and doors open, that in itself was sufficient to permit families to reoccupy it with complete immunity.

These facts would seem to have been recognized and acted upon centuries ago, for in what are the first serious general enactments against the Plague, the orders of the Privy Council promulgated in 1605 and brought into force rigorously in 1665, searchers were appointed to detect cases of Plague by house to house visitation; infected houses were marked and guarded, their inhabitants isolated under compulsion and prevented from leaving within a period of six weeks—a “true quarantine.” In short the “Leicester System” was here for the first time introduced, and Defoe devotes many pages to show how impossible it was. Such isolation is only possible when an epidemic has been detected at its very onset and the affected households are very few in number, and even then can only be enforced when the population is awake to its importance.

What then is to be done? If as already stated the disease be immediately detected, the sick must as immediately be separated from the apparently healthy members, for once it enters a household, surely and not too slowly the tendency is for the members to be affected. But also those of the household who are apparently healthy must be segregated, and inoculated with Haffkine's vaccine, the house disinfected and kept empty for three weeks or more. Segregation was easy of accomplishment in India. There, thanks to the warm climate, whole villages, nay, whole towns, could be turned out of doors into temporary tents and huts. Here, and in European countries, such segregation would present almost insuperable difficulties, while, as Hankin has pointed out to me, it is by no means certain that we could so surely disinfect our many storied and solidly built houses with the same thoroughness with which they disinfected the one or two-roomed hovels in the East with their solid floors and absence of crannies. It comes to this, therefore, that as in the case of small-pox, vaccination so soon as the Plague is heralded in a community, is a sounder hygienic measure than is segregation.

PREVENTIVE INOCULATION :

We owe to Haffkine the discovery as well as the employment upon a very large scale, of the method of vaccination against this disease. Previous experience has shown that preventive inoculation may be produced either by the setting up of a mild form of the disease, or again by introducing dead microbes in their culture media into the system, when the organism reacts against the products of the bacteria which gradually diffuse out of them in the same way as it reacts against the products that are produced when yet they are alive; lastly, one may employ the products which by chemical methods have been separated from the bodies of the bacteria and from the culture fluids in which they have grown.

In connection with cholera, Haffkine found that he could employ the actually living bacteria which, inoculated under the skin, lead only to local effects but confer a general immunity. In connection with Plague this cannot be done with safety, hence he was obliged to employ a method which has not such lasting effect or results, but which nevertheless, is effective—that of inoculating the dead bacilli—and he used the dead bacilli plus the broth in which they had grown rather than this broth alone free from the dead bacilli, because it has been found that the toxic substances formed by this germ only diffuse out very slowly and as these are difficult to separate from the bodies, this inoculation of the bacilli themselves seems to be the simpler process and one likely to yield results most nearly corresponding to those brought about in the actual disease.

Balfour Stewart has recently pointed out that the fluid of growth contains substances which to some extent neutralize the toxins contained in the bacilli themselves, thus indicating a sound reason for Haffkine's procedure, the reaction not being so severe when this fluid is injected along with the bodies of the bacilli, while the immunizing effects are equally potent.

It is unnecessary here to enter into the exact method employed by Haffkine in preparing his fluid, nor again does time or space permit that we should give here a detailed account of the methods employed by Haffkine to test the value of that fluid. We have referred to this previously in this Journal; suffice to say that the latter methods were so complete that in some cases Haffkine was able to inoculate half the population of a village, leaving the other half uninoculated. In every case, except that of the Bulsar inoculation, the treatment has had a considerable effect in warding off plague attacks from the inoculated and in every case, without exception, it has rendered attacks among the inoculated less fatal than the attacks among the uninoculated. Thus comparing 20,225 uninoculated inhabitants of Plague stricken districts

with 22,967 who had been inoculated, the number of Plague deaths among the former was 980, among the latter 118, or, the percentage of death was 4.8 uninoculated and 0.5 inoculated. In other words, the uninoculated had a mortality nine times greater than the inoculated.

As pointed out by the Indian Plague Commission, Haffkine's system cannot as yet be regarded as complete, nevertheless this Commission (which throughout its report assumes a curiously hostile tone) can only conclude that the inoculation sensibly diminishes the incidence to Plague attacks and Plague deaths; that it confers protection which certainly lasts for some considerable number of weeks, possibly for a number of months. They point out that it is generally recognized that within the first week or first few days after the inoculation has been performed, it does not appear to confer any great degree of protection and that yet better results will be obtained when an accurate method of standardizing the fluid has been devised. It may, indeed, be said that not only is inoculation not protective during the first week or so after the operation, but actually there may be increased danger, provided that the individual is already infected, for inoculation definitely adds to the amount of toxic substances circulating in the system. But this is only what has long been recognized in connection with vaccination against small-pox. It is evident that a certain amount of time is necessary for the reaction on the part of the tissues to develop itself and for immunity to be produced, but this fact is no argument against the anti-Plague inoculation during periods when Plague is epidemic any more than it is an argument against vaccinating when there is a threatened epidemic of small-pox in a community.

With regard to standardizing the fluid, Lustig and Galeotti have developed a method which seems as though it may give much more constant results, though possibly the extent of immunity conferred by it may not be so prolonged as by means of Haffkine's original fluid. Employing Buchner's method they treat cultures of the bacilli with caustic potash and thus dissolve out the bacteria and obtain eventually their nucleo-proteids. The substance thus gained is extremely toxic for several animals when employed in any quantity. It can be dried and kept for considerable periods, can be dissolved in a solution of carbonate of soda and injected under the skin. By inoculation of small quantities of this, they were able at Bombay to immunize rats, guinea pigs, rabbits and monkeys. They found further that the immunizing substance was innocuous in the case of man, no troubles of any kind arising from the come contaminated. The exact dose can easily be determined and used without difficulty which is not the case with Haffkine's liquid. Thus we await with considerable interest to see the effect of these nucleo-proteids when applied to those in a Plague district.

Inoculation. In addition, in this dried state it cannot easily be-